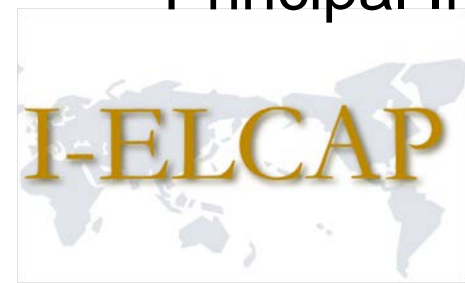


**Centers for Medicare and Medicaid Services
Medicare Evidence Development and Coverage
Advisory Committee Panel
April 30, 2014**

**LUNG CANCER SCREENING WITH LOW-
DOSE COMPUTED TOMOGRAPHY**

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Disclosures



Professor of Radiology, Icahn School of Medicine at Mount Sinai, NY

- I am a named inventor on a number of patents and patent applications relating to the evaluation of pulmonary nodules on CT scans of the chest which are owned by Cornell Research Foundation (CRF).
- As of April 2009, I signed away any financial benefit including royalties and any other proceeds related to the patents or patent applications owned by CRF.

 Principal Investigator of ELCAP, NY-ELCAP, and I-ELCAP

 President of the Early Diagnosis and Treatment Research Foundation






- Funding comes from a variety of sources including philanthropic donations, grant and contracts (federal and non-federal), imaging and pharmaceutical companies related to image processing assessments. The various sources of funding exclude any funding from tobacco companies or tobacco-related sources.



I-ELCAP



To the MEDCAC Panel

-  I am pleased to be part of the consensus of expert opinion and to share results of our 20 years of effort in the development and implementation of CT screening for lung cancer.
-  I will highlight how our long-standing registry has contributed to screening management and integration of advances in technology and knowledge, and can be used to answer questions that are posed about wider implementation of screening.
-  Concerns have been raised about the implementation of screening outside of the institutions participating in the NLST
-  Fortunately we have almost two decades of data collection and experience to respond to each of these concerns through I-ELCAP
-  Moving forward, I-ELCAP looks to coordinating with ACR, STS, LCA and other signatories of the joint consensus letter to provide continuous quality assessment and recommend further refinements of the screening process.



To the MEDCAC Panel

Concerns have been raised about:

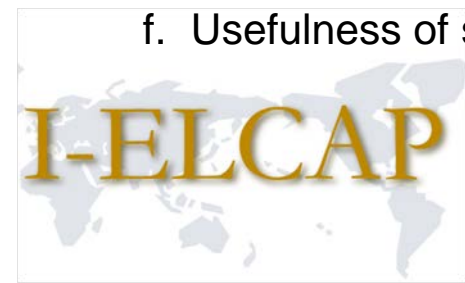
1. External validity of the NLST results:

The external validity of the NLST results have been demonstrated by I-ELCAP. The participating institutions I-ELCAP – both in academic and community settings – have provided prospective registration of each participant, screening following a common protocol which provides the definition of positive results, recommended work-up, and long-term follow-up.

2. Our evidence shows that screening is being done as well at community as at academic centers.

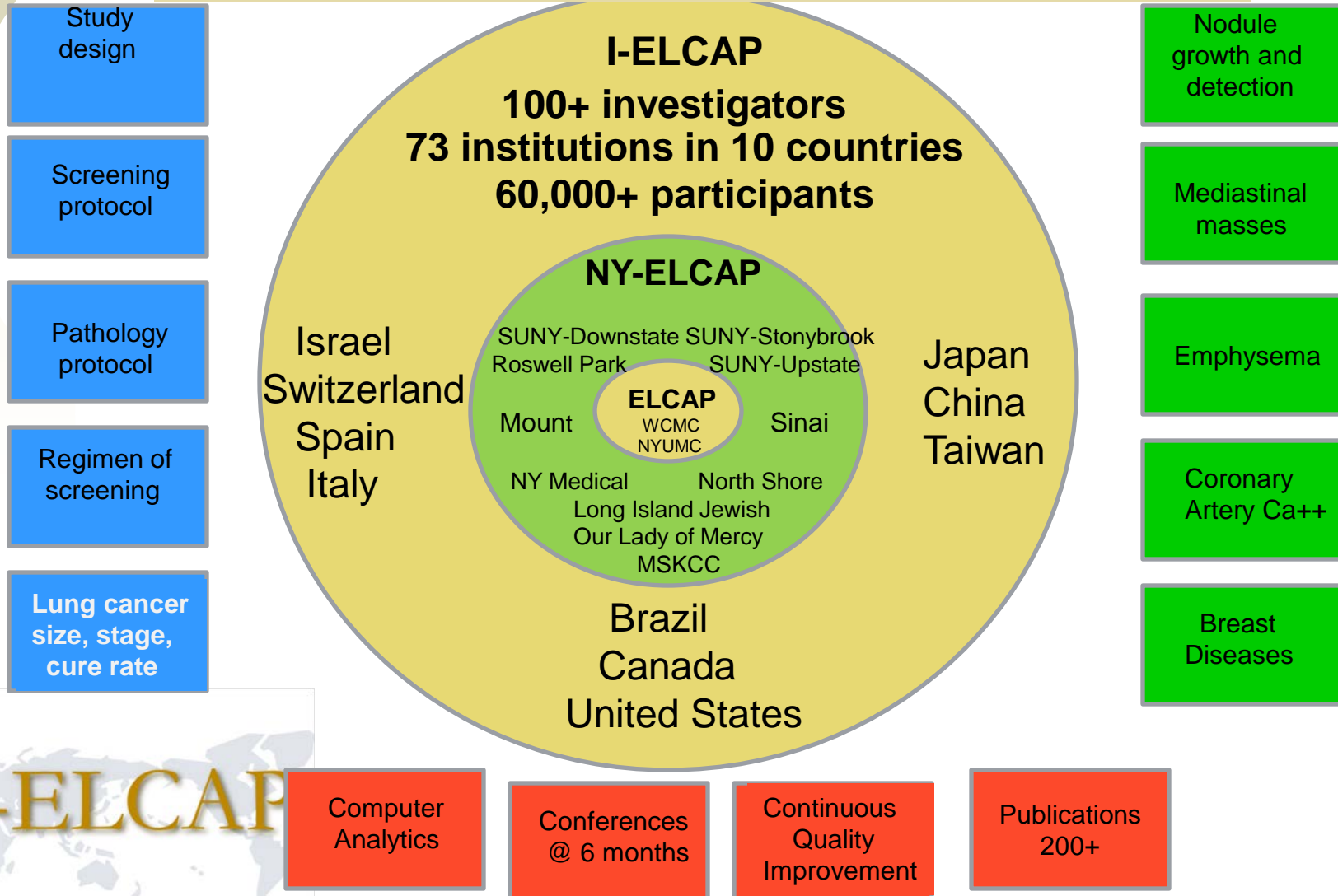
3. I-ELCAP publications have shown that:

- a. Rates of positive results can be kept reasonably low
- b. Those who require workup for positive result, typically require another low-dose CT scan
- c. Invasive procedures are reserved for participants with very suspicious nodules
- d. Surgery for non-malignant disease can be kept low
- e. Smoking cessation information should be provided at time of screening
- f. Usefulness of structured reporting and documentation









ELCAP to NY-ELCAP to I-ELCAP

Registered all baseline, repeat CT screenings, and follow-up
in the past 20+ years conducted at participating institutions
Current, former, and never smokers 40+ years of age



I-ELCAP

-  Is an ongoing registry of **all** screenings at participating institutions using a **common protocol** which has been regularly updated since start of screening in 1992
-  It has a web-based infrastructure which provides **structured** data forms for documentation of the imaging, biopsy, and treatment
-  Quality assurance process is incorporated into the web-based infrastructure
-  Provides formalized training of participating radiologists (dual readings with comparison of discrepancies, status and follow-up reports)
-  The I-ELCAP registry will provide its infrastructure to the Registry for Excellence in Screening led by the LCA and its participating institutions within the Framework of Excellence in Screening.
-  I-ELCAP is collaborating with the LCA, Society of Thoracic Surgery and their registry, and the American College of Radiology to responsibly provide screening throughout the US and to reduce disparities.

I-ELCAP



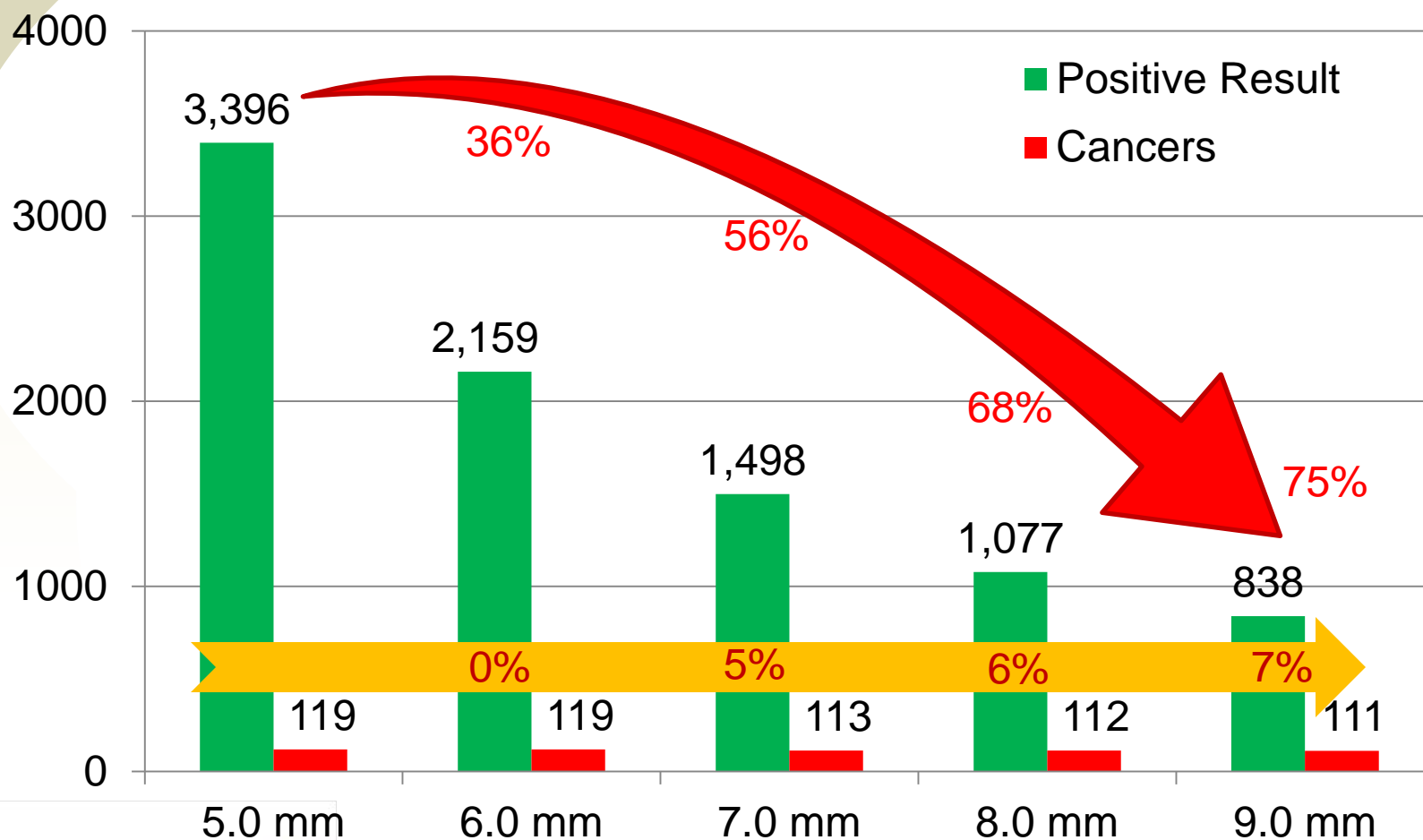
Definition of positive result and workup

- Examined how to reduce the frequency of positive result in the baseline round while having a high proportion in Stage I based on structured reporting and 15 yrs. followup
 - Published in Ann Intern Med. 2013; 158:246-52 and NCCN guidelines changed its threshold to the 6 mm one in 2013.
- Using the NLST database, we have shown that the resulting proportional reductions in positive results going from 5 mm to 9 mm is similar to that published using I-ELCAP data
 - CT Screening for Lung Cancer: Alternative Definitions of Positive Test Result Based on the National Lung Screening Trial Database. Radiology 2014. Accepted

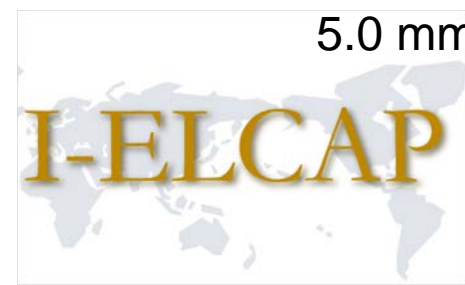
I-ELCAP



Baseline: frequency of positive result and dx of lung cancer among 21,136 recent participants



Henschke CI, Yip R, Yankelevitz DF et al. Definition of a positive test result in computed tomography screening for lung cancer: a cohort study. Ann Intern Med. 2013; 158:246-52.



I-ELCAP: Definition of + results and workup

Baseline Round of Screening – UPDATED 2014

1. Follow-up in 1 year (first annual repeat screening), if

Negative: No NCN (noncalcified nodules)

Semi-positive: Largest part-solid or solid NCN < 6 mm in avg. diameter

Semi-positive: Nonsolid NCN of any size

2. Follow-up CT scan in 3 months, if

Positive: Largest part-solid or solid NCN 6-14 mm in avg. diameter

Suspicious: Growth** at a malignant rate on 3 mos. f-up CT

3. Immediate workup (PET, Bx, or 1 month f-up CT), if

Suspicious: If largest part-solid or solid NCN \geq 15 mm in avg. diameter

* if NCN \geq 10 mm and very suspicious in appearance, immediate PET scan is an option. Note that hamartomas and granulomas are typically of this size

**The solid component of the NCN is measured, growth is at a malignant rate if the relative change in volume is more than:

a) 65% for nodules 3-6 mm; b) 50% for nodules 6-7 mm; c) 40% for nodules 8-9 mm; d) 30% for nodules > 10 mm

I-ELCAP: Definition of + results and workup

Each Annual Repeat Round of Screening – NO CHANGE

1. Follow-up in 1 year (next round of annual repeat screening), if

Negative: No new or growing NCN

Semi-positive: Largest new part-solid or solid NCN < 3 mm in avg. diameter

Semi-positive: New nonsolid NCN of any size

2. Follow-up CT scan in 6 months, if

Positive: New or growing part-solid or solid NCN 3-6 mm in avg. diameter

Suspicious: Growth** at a malignant rate on 6 mos. f-up CT

3. Follow-up CT in 1 month, if

Positive: New or growing part-solid or solid NCN \geq 6 mm in avg. diameter

Suspicious: If growth** at a malignant rate on 1 mo. f-up CT

NOTES from protocol (www.ielcap.org)

* if NCN \geq 10 mm and very suspicious in appearance, immediate PET scan is an option. Note that hamartomas and granulomas are typically of this size

**The solid component of the NCN is measured, growth is at a malignant rate if the relative change in volume is more than:

a) 65% for nodules 3-6 mm; b) 50% for nodules 6-7 mm; c) 40% for nodules 8-9 mm; d) 30% for nodules > 10 mm

For detailed description, see I-ELCAP protocol (www.IELCAP.org), pages 7 and 8.

Any screening participant diagnosed with lung cancer and treated for curative intent should continue with annual CT screening

The I-ELCAP Registry allows for continual updates to protocol and assessment of the benefit

Respond to rapid advances CT technology

- From 1-slice to 256+slice, dual source scanners

Development of computer assisted diagnostics

Integrate emerging information

- Introduction of PET scans into workup
- Nodule growth
- Updates to definition of positive result (see updated recommendations for baseline round of screening) based on analysis of I-ELCAP and NLST data.



Frequency of + result at baseline (B) and annual repeat (A) rounds and resulting Stage I and estimated cure rate

 I-ELCAP all: participants aged 40 and older

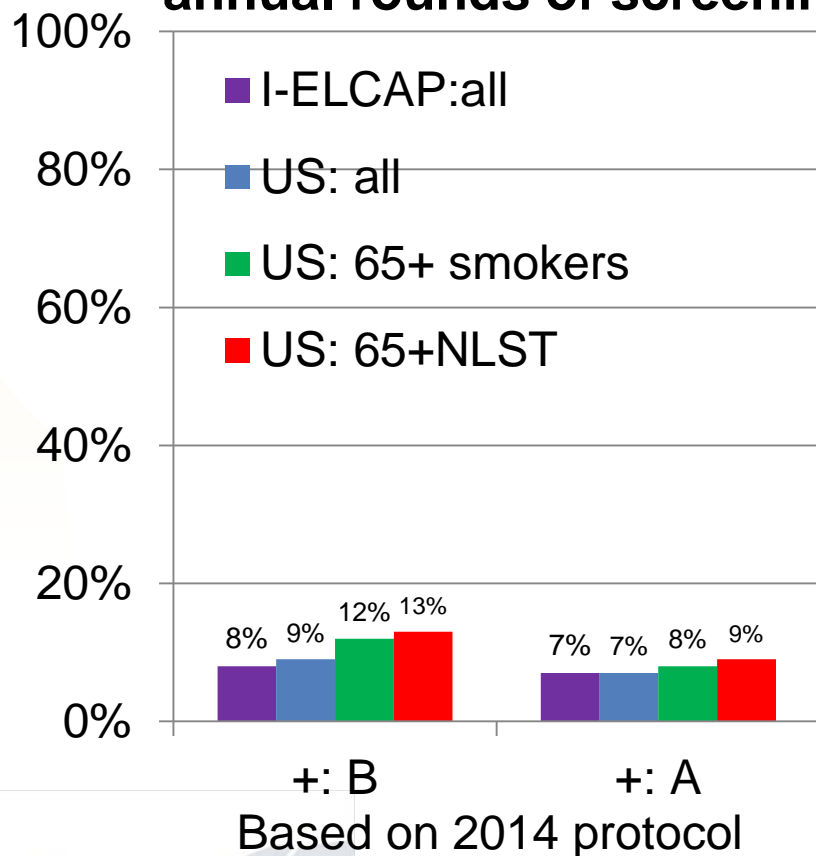
 US institutions only:

- All: current, former, never smokers aged 40 and older
- 65+ smokers: all current and former smokers who are 65 years of age and older
- 65+NLST: NLST criteria (current smokers and former smokers who quit within the last 15 years) who are 65+ years of age or older

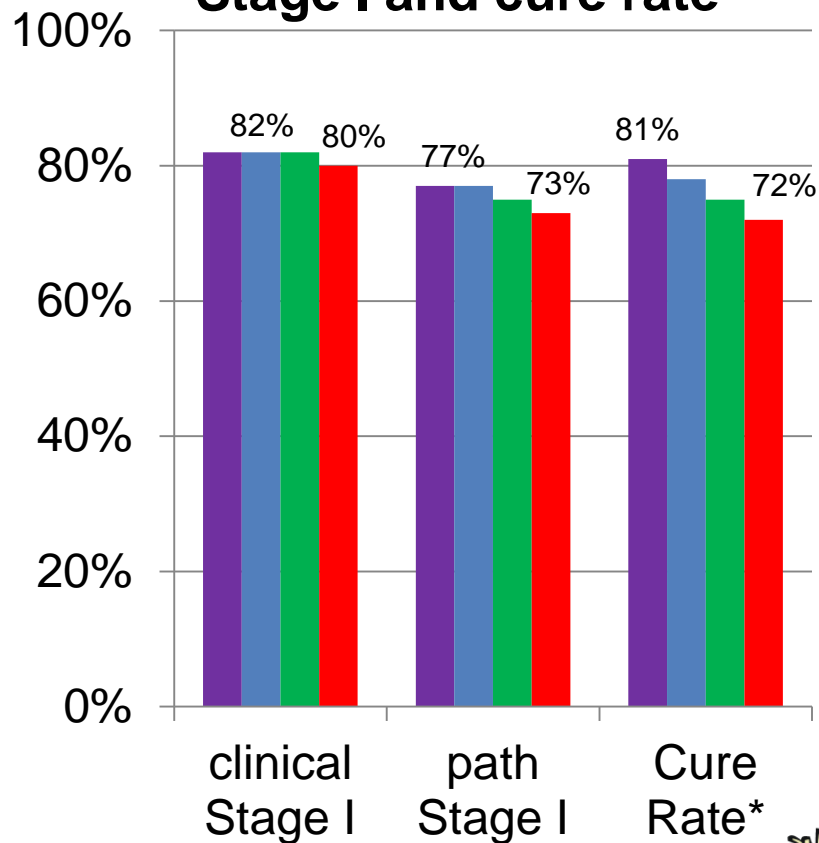


Frequency of + result at baseline (B) and annual repeat (A) rounds and resulting stages and estimated cure rates

+ Result in baseline and annual rounds of screening



Clinical, pathologic Stage I and cure rate*



*Cure rate estimated by 15-year survival rate



US Academic vs. Community Setting



No differences* in the

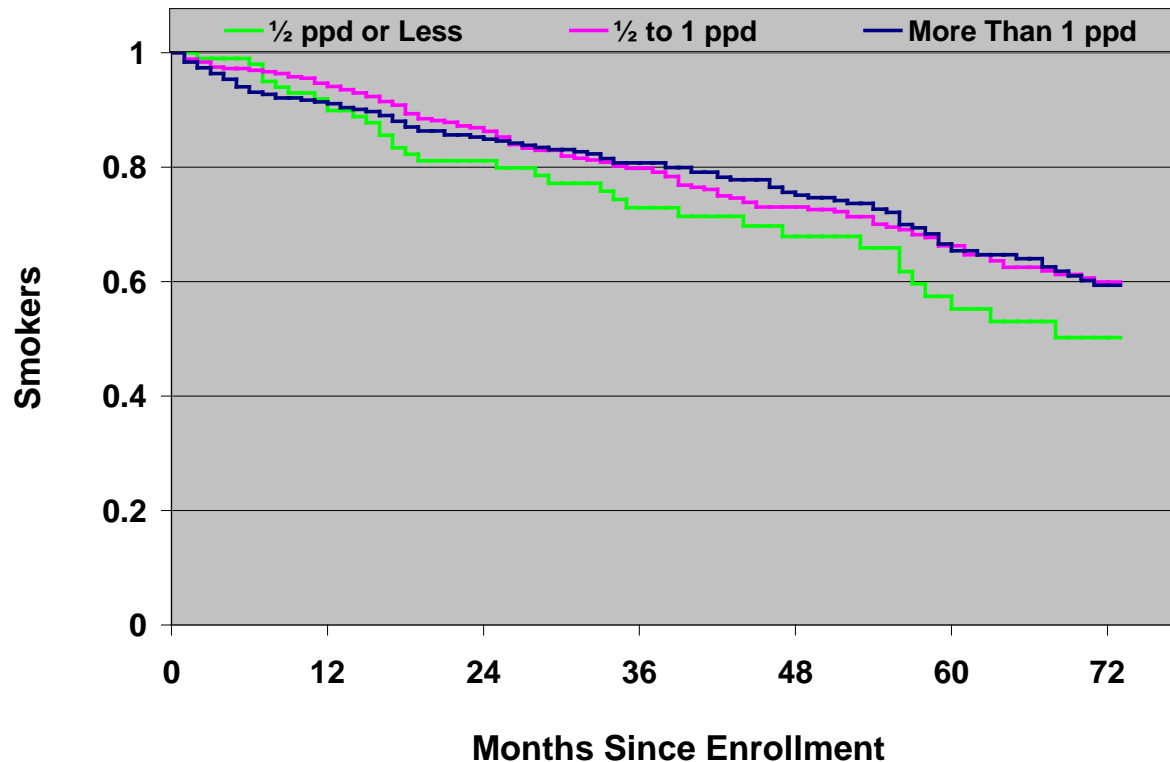
- Frequency of positive findings on baseline and on annual repeat screening
- Frequency of Stage I
- Estimated cure rates (based on 15 year Kaplan-Meier survival rates)



*Based on logistic and Cox regression analyses



Over time, more and more smokers quit when enrolled in a program of CT screening for lung cancer.



Anderson et al. Cancer Epidemiol Biomarkers Prev 2009; 18: 3476-83



Summary



Focusing on 65+ year old smokers

- Positive rates can be kept reasonably low
- Unnecessary imaging and surgery can be minimized (i.e., kept at lower rates than currently found in routine clinical care)
- Cure rates are high ($> 70\%$) as compared to when there is no screening ($< 10\%$)



Results are similar for smokers aged 65 and older, even at lower pack-years of smoking and longer years of quitting



No difference in screening results at academic and community institutions in I-ELCAP



CT screening does not lead to resumption of smoking



Importance of Each Additional Round of Annual Repeat Screening



Each round of annual repeat screening will result in new diagnoses of lung cancer at essentially the same frequency.

- The 3 years in the NLST were chosen to reduce the cost and time for the study.
 - As soon as the screening stopped, the proportion in Stage I started to decrease towards what it was in the absence of screening.
 - This is clearly illustrated by the NLST results (NEJM, Table 5).

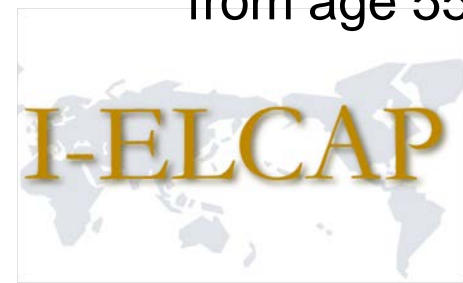


USPSTF recommended providing annual screenings from age 55 to 80 (i.e., a baseline and 24 annual repeat rounds). Focusing only on annual rounds, a simplified way of stating the benefit is:

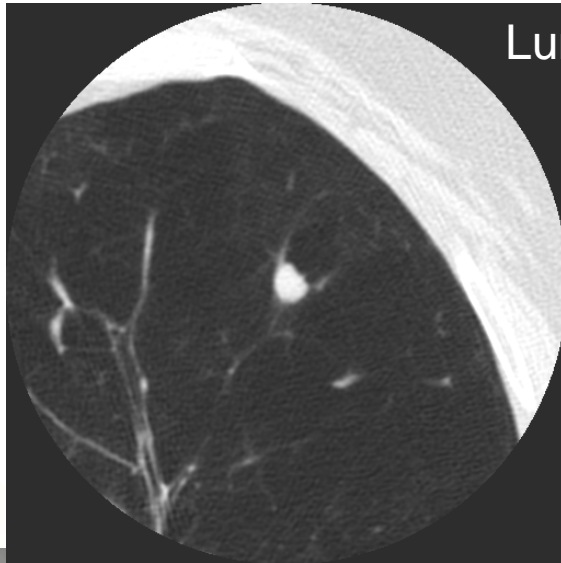
- If an annual repeat round saves L lives, then 24 years of annual screening will save $24 \times L$ lives
- NLST had 2 annual repeat rounds (baseline and 2 annual rounds) and these rounds saved $2 \times L$ lives.



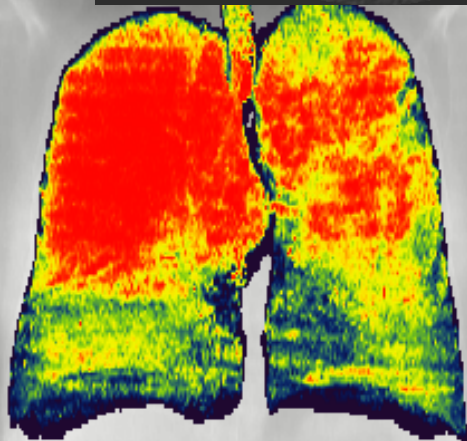
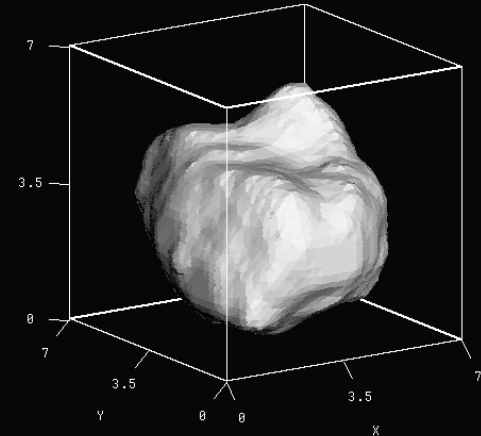
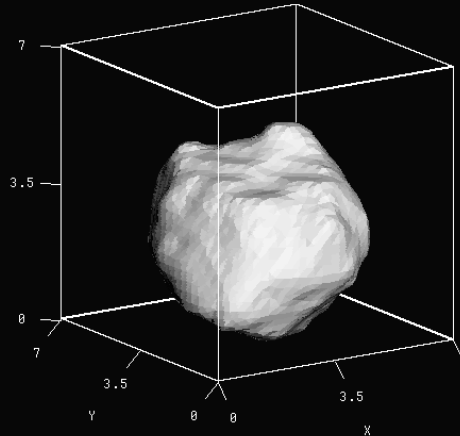
This is the basis for the USPSTF recommending annual screening from age 55 to age 80.



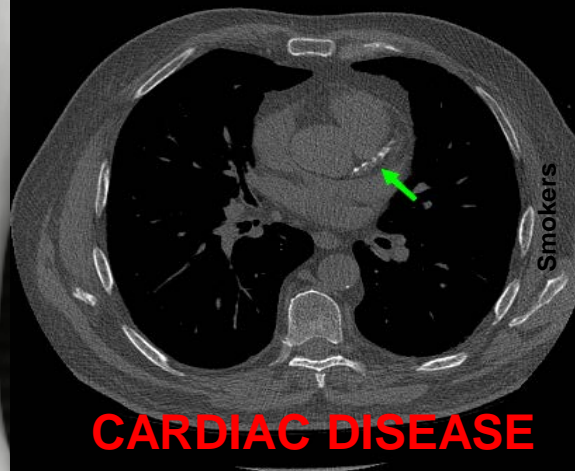
LOW-DOSE CT SCREENING



Lung Cancer and Volume Doubling Times



EMPHYSEMA



CARDIAC DISEASE

